Electronic supplementary information (ESI)

Mesoporous polydopamine nanoparticles with co-delivery function for overcoming multidrug resistance via synergistic chemo-photothermal therapy

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**Particle characterizations.**

Transmission electron microscope (TEM) images were obtained by a JEM 2010 (JEOL, Japan) instrument with 200 KV acceleration voltages. Samples were dried on carbon-coated Cu grids.

Scanning electron microscopy (SEM) measurements were performed with a JSM-7800F field-emission scanning electron microscope (SEM, JEOL, Japan).

Nitrogen sorption isotherms were measured with a ASAP2010 analyzer (Micromeritics, USA). The specific surface areas were calculated by the Brunauer-Emmett-Teller (BET) method in a linear relative pressure range between 0.05 and 0.25. The pore size distributions were derived from the desorption branches of the isotherms by the NLDFT method.

The hydrodynamic size distributions and zeta potentials of the samples were measured using dynamic light scattering (DLS) techniques by a Zetasizer Nano instrument (Malvern, UK) at 25 °C.

Thermogravimetric analysis (TGA) was conducted with a Q500 instrument (TA Instruments, USA). The materials were tested under an air atmosphere from 30 °C to 900 °C at a heating rate of 10 °C min⁻¹.

The fluorescence emission of the DOX and DOX loaded MPDA solution was measured by using a fluorescence spectrophotometer (RF-6000, Shimadzu).
Fig. S1 Scanning electron microscopy (SEM) image of the prepared MPDA nanoparticles.
Fig. S2 (a) Zeta potentials (measured in HEPES buffer, pH 7.4) MPDA, MPDA-DOX and MPDA-DOX@TPGS, MPDA particles after treatment with TPGS solution in the loading buffer (HEPES, 25 mM, pH 7.4) with the presence of 10 vol% acetone, and MPDA particles after treatment with TPGS solution in the loading buffer (HEPES, 25 mM, pH 7.4) without acetone. (b) thermogravimetric curves of MPDA, MPDA-DOX and MPDA-DOX@TPGS measured in air atmosphere. (c) Transmission electron microscope (TEM) image of MPDA-DOX@TPGS.
Fig. S3 Hydrodynamic diameter distributions of MPDA, MPDA-DOX, and MPDA-DOX@TPGS in HEPES buffer (25 mM, pH 7.4), determined by dynamic light scattering (DLS).
**Fig. S4.** (a) Temperature elevation profiles of MPDA particle suspensions (200 μg mL⁻¹) as a function of irradiation time. Different laser power densities (0.5, 1, 1.5 and 2 W cm⁻²) were employed for comparison, and the irradiation lasted for 20 min. (b) UV-vis absorption spectra of MPDA dispersion (200 μg mL⁻¹) in water. (c) Photothermal effect of the irradiation of the aqueous dispersion of MPDA (200 μg mL⁻¹) with the 808 nm NIR laser (2 W cm⁻²). The irradiation lasted for 22 min, and then the laser was turned off. (d) Plot of cooling time versus negative natural logarithm of the temperature driving force (∆T/∆T_{max}) in the cooling stage. The thermal time constant for heat transfer from the system is determined to be τ_s = 227 s.

The photothermal conversion efficiency (η) of MPDA was determined to be 12.8% according to the following equation used in the reported studies:⁴ ⁵

\[
\eta = \frac{hS(T_{max} - T_{surr}) - Q_0}{I(1 - 10^{-\Delta T/T_{max}})} = \frac{hS(T_{max} - T_{surr}) - hS(T_{max, water} - T_{surr})}{I(1 - 10^{-\Delta T/T_{max}})} \quad (1)
\]

Where \( h \) is the heat transfer coefficient, \( S \) is the sample container surface area, \( T_{max} \) is the steady state maximum temperature of water (45.5°C), \( T_{max, water} \) is the steady state maximum temperature
of water (26.7 °C), \( T_{\text{sur}} \) is the ambient room temperature (21.3 °C), \( Q_0 \) is the background energy input by the solvent and the sample container without the presence of MPDA, \( I \) is the laser power, and \( A_{808} \) is the absorbance of MPDA at 808 nm (1.64). The value of \( hS \) is calculated by equation 2:

\[
\tau_s = \frac{m_d C_d}{hS} \quad (2)
\]

Where \( \tau_s \) is the characteristic thermal time constant determined from the curve in \textbf{Fig. S4} (227 s), \( m_d \) is the mass of the nanoparticle solution (0.3 g), and \( C_d \) is the heat capacity which was approximated to be 4.2 J g\(^{-1}\) K\(^{-1}\) (the heat capacity of water).
**Fig. S5** Confocal laser scanning microscopy (CLSM) images of MCF-7/ADR cells incubated with MPDA (20 μg mL⁻¹ for 4 h) in the absence (a) or presence of pre-treatment with different specific endocytotic inhibitors (b, 20 μg mL⁻¹ of nystatin for 2 h; c, 10 μg mL⁻¹ of chlorpromazine for 2 h).

The concentrations of the inhibitors were chosen based on previous studies.¹⁻³ The scale bar represents 7.5 μm.
Fig. S6 Confocal laser scanning microscopy (CLSM) images of MCF-7/ADR cells incubated with MPDA (20 μg mL⁻¹). From left to right, (a) bright field (with white arrows indicating internalized MPDA nanoparticles), (b) cell endosomes stained LysoTracker green (a fluorescent marker of acidified vesicles), (c) the merge of the two images. The scale bar represents 25 μm.
**Fig. S7** Confocal laser scanning microscopy (CLSM) images of MCF-7/ADR cells incubated with calcein loaded MPDA (20 μg mL\(^{-1}\)) for 36 h. From left to right, (a) calcein’s green fluorescence channel, (b) cell endosomes stained LysoTracker Red (a fluorescent marker of acidified vesicles), (c) the merge of the two images. The scale bar represents 25 μm.
References.


